FIG. 35A-35B. Nucleotide sequence of pRIG22. (SEQ ID NO.: 27).

On page 30, please replace the sentence on line 9 with the following sentence:

FIG. 37A-37C. Nucleotide sequence of pRIG-T (SEQ ID NO:28).

REMARKS

Reconsideration of this Application is respectfully requested. The specification has been amended to incorporate sequence identification numbers and to correct a typographical error. The Sequence Listing and Computer Readable Copy have been submitted in accordance with 37 C.F.R.§ 1.821. The amendments have been made to further prosecution in this application. No new matter has been added, thus, entry of the amendments is respectfully requested.

CONCLUSION

It is believed that a full and complete response has been made to the Notice and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

SHANKS & HERBERT

By: _____
Joseph G. Contrera
Reg. No. 44,628

Date: 10/29/02

TransPotomac Plaza
1033 N. Fairfax Street, Suite 306
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MARKED-UP VERSION OF THE AMENDMENTS

In the Specification:

Please put a period after the text in lines 10 and 11 on page 130 as follows:

(g) Incubate at 4°C (hold).

(h) END.

Please put a period after the text in line 22 on page 134 as follows:

(ii) 30 cycles of 92°C denaturation for 15 sec; 60°C primer annealing for 20 sec; and 72°C primer extension for 40 sec.

Please put a period after the text in line 30 on page 140 as follows:

35) After binding collect SA-PMPs through use of a magnet and recover flow through material (SAVE THIS MATERIAL!).

On page 17, please replace the paragraph in lines 10-19 with the following paragraph:

FIG. 1. Schematic diagram of gene activation events described herein. The activation construct is transfected into cells and allowed to integrate into the host cell chromosomes at DNA breaks. If breakage occurs upstream of a gene of interest (e.g., Epo), and the appropriate activation construct integrates at the break such that its regulatory sequence becomes operably linked to the gene of interest, activation of the gene will occur. Transcription and splicing produce a chimeric RNA molecule containing exonic sequences from the activation construct and from the endogenous gene. Subsequent translation will result in the production of the protein of interest. Following

isolation of the recombinant cell, gene expression can be further enhanced via gene amplification. The polyA tail is set forth in SEQ ID NO:33.

On page 21, please replace the paragraph in lines 6-17 with the following paragraph:

FIG. 13. Illustration depicting two transcripts produced from the integrated vectors described in Figures 12A-12G. DNA strands are depicted as horizontal lines. Vector DNA is shown as a black line. Endogenous genomic DNA is shown as a grey line. Rectangles depict exons. Vector-encoded exons are shown as open rectangles, while endogenous exons are shown as shaded boxes. S/D denotes a splice donor site. Following integration, the vector encoded promoters activate transcription of the endogenous gene. Transcription resulting from the upstream promoter produces a spliced RNA molecule containing the vector encoded exon joined to the second and subsequent exons from an endogenous gene. Transcription from the downstream promoter, on the other hand, produces a transcript containing the sequences downstream of the integrated DNA joined to exon I and the subsequent exons from an endogenous gene. The polyA tails are set forth in SEQ ID NO:33.

On page 26, please replace the paragraph in lines 6-25 with the following paragraph:

FIG. 23A-23D. Example of a multi-Promoter/Activation Exon Vector. Each vector is illustrated schematically in its linearized form. Each horizontal line represents a DNA molecule. The arrows denote promoter sequences. Boxes indicate exons. Hatched

boxes indicate untranslated regions. It is understood that the exons on these vectors may be untranslated, or may contain a start codon and additional codons as described herein. The following designations were used: splice donor site (S/D), vector promoter #1 (VP #1), vector promoter #2 (VP #2), vector promoter #3 (VP #3), and vector promoter #4 (VP #4). Individual vector activation exons are designated A, B, C, and D (SEQ ID NOS: 29-32, respectively). Each activation exon may contain a different structure. The structure of each activation exon and its flanking intron are shown below. It is understood, however, that any activation exon described herein, may be used on these vectors, in any combination and/or order, including exons that encode signal sequences, partial signal sequences, epitope tags, proteins, portions of proteins, and protein motifs. Any of the exons may lack a start codon. In addition, while not illustrated in these examples, these vectors may contain a selectable marker and/or an amplifiable marker. The selectable marker may contain a poly (A) signal or a splice donor site. When present, the splice donor site may be located upstream or downstream of the selectable marker. Alternatively, the selectable marker may not be operably linked to a poly (A) signal and/or a splice donor site.

On page 29, beginning at line 19, lines 19-25 have been replaced with the following lines:

FIG. 29A-29B. Nucleotide sequence of pRIG14. (SEQ ID NO: 21).

FIG. 30A-30C. Nucleotide sequence of pRIG19. (SEQ ID NO.: 22).

FIG. 31A-31C. Nucleotide sequence of pRIG20. (SEQ ID NO.: 23).

FIG. 32A-32C. Nucleotide sequence of pRIGad1. (SEQ ID NO.: 24).

FIG. 33A-33D. Nucleotide sequence of pRIGbd1. (SEQ ID NO.: 25).

FIG. 34A-34B. Nucleotide sequence of pUniBAC. (SEQ ID NO.: 26).

FIG. 35A-35B. Nucleotide sequence of Prig22. (SEQ ID NO.: 27).

On page 30, please replace the sentence on line 9 with the following sentence:

FIG. 37A-37C. Nucleotide sequence of pRIG-T (SEQ ID NO:28).